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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/640,952	08/17/00	KINCH	M 3220-66872

HM12/0705

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EXAMINER	
DAVIS,N	
ART UNIT	**PAPER NUMBER**
1642	7

DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/640,952	Applicant(s) KINCH ET AL.	
	Examiner Natalie A Davis	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,21-24 and 28-71* is/are pending in the application.

4a) Of the above claim(s) *14-20,25-27 and 72-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,21-24 and 28-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, 21-24, and 28-71, drawn to a method of detecting metastatic cells, classified in class 435, subclass 7.1.

II. Claims 14-16, and 89, drawn to a method of producing an antibody, classified in class 530, subclass 387.1.

III. Claims 17-20, 25-27, and 84-88, drawn to an antibody and kit, classified in class 530, subclass 387.9.

IV. Claims 72-81, drawn to a method detecting cancer cells, classified in class 435, subclass 7.1.

V. Claims 82-83, drawn to the D7 hybridoma cell line, classified in class 435, subclass 326.

The inventions are distinct, each from the other because of the following reasons:

2. The Inventions of Groups III and V (products) and I-II, and IV (methods) are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products of Groups III and V may be used for a number of different processes that are very much unrelated. For example, the antibody of Group III may not only be used in the method of Group I, but may also be used for immunopurification.

3. The products of Groups III and V are drawn to structurally and functionally different molecules with different immunological properties, each invention requires different reagents and steps to make and characterize it.

4. The methods of Groups I-II, and IV relate to methods, but each method differs in method steps, modes of operation, reagents needed and serve different endpoints and effect.

5. Inventions II and III are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the method of Group II may be used to isolate an antibody that is structurally and functionally different than the antibody of Group III.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, divergent subject matter, and require different search strategies, restriction for examination purposes as indicated is proper.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

8. During a telephone conversation with Attorney Sandberg on 18 May, 2001 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-13, 21-24, and 28-71. Affirmation of this election must be made by applicant in replying to this Office action. Claims 14-20, 25-27, and 72-89 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

9. The information disclosure statements filed 20 February and 16 March, 2001 have been considered. A signed copy is attached hereto.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10-13, 21-24, and 28-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pasquale, et al., (1995) in view of Zantek, et al., (1998) and Kinch, et al., (1998). The elected claims are drawn to a method for detecting the presence of metastatic cells comprising lysing cells, incubating cells with a reagent capable of specifically binding to the epitope of EphA2 to allow antibody binding, and detecting compound-epitope binding.

Pasquale, et al., teach a method of diagnosing cancer and determining cancer prognosis wherein, the level Eph-related protein tyrosine kinase in a sample as compared to a normal sample is indicative of the presence of a cancer or the level of malignancy of a cancer and methods of determining Eph-related kinases using RNA and protein blot analysis, ELISA, using specific antibodies to the Eph-related kinase (col. 9). Pasquale, et al., does not teach to use a reagent that specifically binds the EphA2 epitope. Zantek, et al. teach the EphA2 receptor tyrosine kinase as a marker for breast cancer progression and that normal breast epithelial express tyrosine phosphorylated EphA2, while weakly invasive cells lose expression and metastatic cells express non-phosphorylated EphA2. Kinch et al., (1998) teach the D7 and B2D6 hybridoma cell line, which produce antibodies that are specific to the EphA2 epitope. In addition to lysing of cells before incubation with a reagent capable of binding to an epitope, fixing cells on a slide before detection with immunofluoresence staining, and detection of an antibody using fluorescence label. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Pasquale, et al., Zantek, et al., and Kinch et al., to use the method as claimed since the references teach that Eph-related tyrosine kinase may be used as an indicator for the presence of metastatic cells. One of ordinary skill in the art would have been motivated to use the claimed method because of the reasonable expectation of success based on well known and accepted methods in the art of how

to determine the expression levels of Eph-related tyrosine kinases and to make an antibody that binds specifically to an epitope (Kinch et al.). Also, to determine these levels using methods well known in the art, as taught by Pasquale, et al., such as ELISA, flow cytometry, western blotting, and antibodies, which would be specific to the EphA2 epitope and fluorescent or radioactive labels, which may be easily detected. Furthermore, it would be obvious to use the method as claimed since it is well known in the art that Eph-related tyrosine kinase expression is related to the progression of cancer. Likewise, since the antibodies produced by the D7 and B2D6 cell lines are specific for the EphA2 epitope, one would expect it to bind to the intracellular epitope of EphA2.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Natalie A. Davis, Ph.D.
July 2, 2001

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